

Amendments to the Claims:

This listing of the claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-2 (Cancelled)

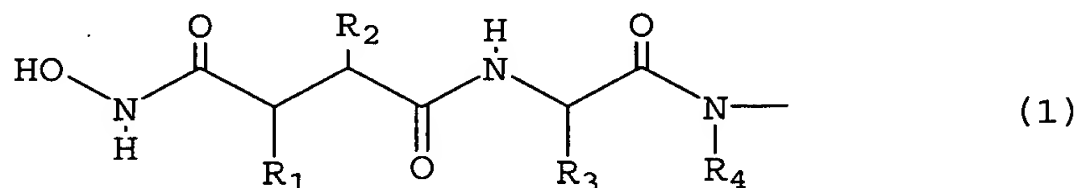
3 (Previously presented). The method of claim 17, wherein the therapeutic agent for joint diseases is a matrix metalloprotease inhibitor.

4 (Cancelled)

5 (Previously presented). The method of claim 3, wherein the weight ratio of the matrix metalloprotease inhibitor to the entire conjugate is 0.01 to 50%.

6 (Previously presented). The method of claim 3, wherein the matrix metalloprotease inhibitor is a hydroxamic acid residue.

7 (Previously presented). The method of claim 3, wherein the matrix metalloprotease inhibitor is a hydroxamic acid residue represented by the general formula (1):



wherein

R₁ is a hydrogen atom, a hydroxyl group or a straight-chain or branched-chain alkyl group having 1 to 8 carbon atoms;

R₂ is a straight-chain or branched-chain alkyl group having 1 to 8 carbon atoms;

R₃ is a straight chain or branched alkyl group having 1 to 8 carbon atoms which may be substituted with a cycloalkyl group, an aryl group or a heterocyclic group; and

R₄ is a hydrogen atom or an alkyl group having 1 to 4 carbon atoms.

8 (Currently Amended). The method of claim 17, wherein the spacer is represented by the general formula (2):



wherein

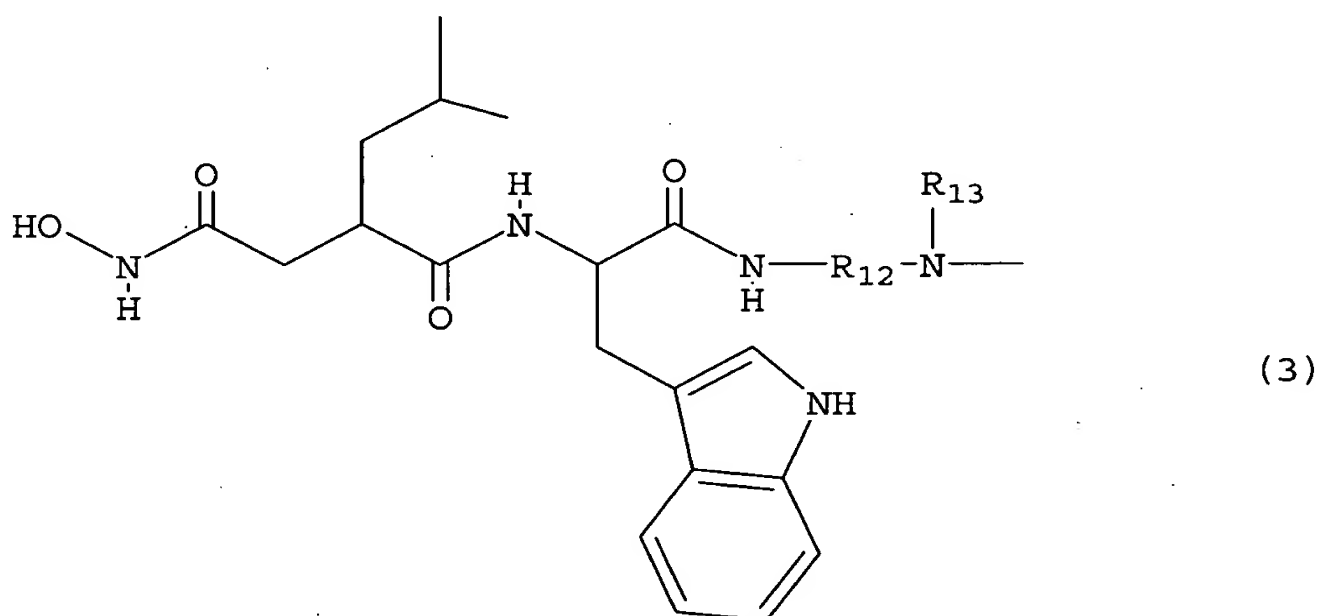
R₅ is a straight-chain or branched-chain alkylene group having 1 to 8 carbon atoms;

R₆ is an oxygen atom or a methylene or imino group which may be substituted with a straight-chain or branched-chain alkyl group having 1 to 4 carbon atoms;

R₇ is a straight-chain or branched-chain alkylene group having 1 to 10 carbon atoms into which one to three oxygen atoms may be inserted; and

~~R₈ is an oxygen atom, a sulfur atom or NR₉~~, wherein R₉ is a hydrogen atom or a straight-chain or branched-chain alkyl group having 1 to 4 carbon atoms.

9 (Previously presented). The method of claim 3, wherein the matrix metalloprotease inhibitor and the spacer constitute a moiety represented by the general formula (3):



wherein

R₁₂ is a straight-chain or branched-chain alkylene group having 2 to 23 carbon atoms into which one imino group and/or one to four oxygen atoms may be inserted; and R₁₃ is a hydrogen atom or a straight-chain or branched-chain alkyl group having 1 to 4 carbon atoms.

10 (Previously presented). The method of claim 3, wherein the matrix metalloprotease inhibitor in the form of a conjugate with hyaluronic acid, a hyaluronic acid derivative or a salt thereof inhibits a matrix metalloprotease *in situ*.

11 (Previously presented). A method for preparing a conjugate of (1) at least one therapeutic agent for joint diseases which is bonded via a spacer to (2) hyaluronic acid, a hyaluronic acid derivative or a salt thereof, wherein a carboxyl group of the hyaluronic acid, derivative or salt, and an amino group of the spacer form an amide bond, comprising binding a site of the therapeutic agent for joint diseases that does not affect the activity of the agent to the hyaluronic acid, derivative or salt, via the spacer.

12-16 (Cancelled)

17 (Previously presented). A method for treating a patient having a joint disease comprising administering to the patient a pharmaceutical composition containing, as the effective ingredient, a pharmaceutically effective amount of a conjugate of (1) at least one therapeutic agent for joint diseases which is bonded via a spacer to (2) hyaluronic acid, a hyaluronic acid derivative or a salt thereof, wherein a carboxyl group of the hyaluronic acid, derivative or salt, and an amino group of the spacer form an amide bond.

18 (Previously presented). The method of claim 17, wherein the therapeutic agent for joint diseases is selected from the group consisting of a cyclooxygenase 2 inhibitor, an antirheumatic agent and a matrix metalloprotease inhibitor.

19-21 (Cancelled)

22 (Previously presented). A method of treating a joint disease in a patient in need thereof, comprising administering a pharmaceutical composition to said patient in an amount sufficient for said treatment, wherein said pharmaceutical composition comprises a conjugate of (1) at least one therapeutic agent for joint diseases which is bonded via a spacer to (2) hyaluronic acid, a hyaluronic acid derivative or a salt thereof, wherein a carboxyl group of the hyaluronic acid, derivative or salt, and an amino group of the spacer form an amide bond.

23 (Previously presented). The method of claim 17, wherein component (1) is a single therapeutic agent for joint disease.

24 (Previously presented). The method of claim 17, wherein component (2) is hyaluronic acid or a salt thereof.

25 (Previously presented). The method of claim 17, wherein the joint disease is selected from the group consisting of osteoarthritis, rheumatoid arthritis, and scapulohumeral periarthrititis.

26 (Previously presented). The method of claim 24 wherein the hyaluronic acid has a weight average molecular weight of 100,000 to 10,000,000.

27 (Previously presented). The method of claim 11, wherein the site of the therapeutic agent for joint diseases

is first bonded to the spacer and then the spacer is bonded to the carboxyl group of the hyaluronic acid, derivative or salt.

28 (Previously presented). The method of claim 11, wherein the binding reaction takes place in an aqueous solution containing 1 to 50% of an organic solvent.

29 (Previously presented). The method of claim 28, wherein the organic solvent is selected from the group consisting of N,N-dimethylformamide, N-methylpyrrolidone, dioxane, ethanol and pyridine.

30 (Previously presented). The method of claim 11, wherein said binding step further includes the addition of an additive for accelerating the binding reaction.

31 (Previously presented). The method of claim 30, wherein the additive for accelerating the binding reaction is selected from the group consisting of N-hydroxysuccinimide, N-hydroxy-5-norbornene-2,3-dicarboximide, p-nitrophenol, pentafluorophenol, 1-hydroxybenzotriazol and 1-hydroxy-7-azabenzotriazol.